

## **REMARKS**

These remarks are responsive to the final Office action dated September 10, 2004. Claims 28-30, 33-41, and 83-89 are pending in the application. Claim 83 is the only independent claim. In the Office action, the Examiner rejected all of the pending claims under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,524,790 to Kopf-Sill et al (“Kopf-Sill”). Applicants disagree. In response to the Office action, applicants are submitting a Request for Continued Examination under 37 C.F.R. § 1.114, and in view of the following remarks, request reconsideration of the application under 37 C.F.R. § 1.111 and allowance of the pending claims. In particular, applicants do not believe that the cited reference discloses each and every limitation of the pending claims.

### ***I. Request for Continued Examination***

Applicant is submitting herewith a Request for Continued Examination (RCE) under 37 C.F.R. § 1.114. This Request complies with the requirements of 37 C.F.R. § 1.114. In particular:

- (i) Prosecution in the application is closed, since the last action was a final Office action under 37 C.F.R. § 1.113.
- (ii) The Request is accompanied by a submission as set forth at 37 C.F.R. § 1.114(c), specifically, the amendments and remarks set forth herein.
- (iii) The Request is accompanied by the fee set forth at 37 C.F.R. § 1.17(e).

Accordingly, applicant respectfully requests grant of this Request for Continued Examination.

## **II. The Claimed Invention**

The application currently includes one independent claim (claim 83) and eighteen dependent claims (claims 28-30, 33-41, and 84-89). These claims are directed to a kit for detecting the presence and/or activity of an analyte in a sample. The claimed kit includes (A) a probe bound to a member, where the member is a compound that specifically binds to the analyte, or is a substrate for the analyte, and (B) a particulate mass label capable of specifically binding to one of the member and the complex formed by binding of the member to the analyte, or one of the member and the product of the action of the analyte on the member. The member-probe combination is adapted such that a measurable property of the probe is sensitive to the size of the complex formed by binding of the mass label and the probe/member, probe/member-analyte complex, or probe/member product. That is, the kit includes at least (A) a probe bound to a member, and (B) a particulate mass label, all selected such that the binding of the particulate mass label alters a measurable property of the probe, so that the binding of the particulate mass label may be detected and/or measured, and optionally related to one or more characteristics of the system under analysis. Significantly, because the probe is bound to the member, the probe is always available (even if it is not always used) in association with the member to report on the size of complexes, if any, involving the member or member product.

## **III. Claim Rejections – 35 USC § 102**

The Examiner rejected all of the pending claims under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,524,790 to Kopf-Sill et al (“Kopf-Sill”). Applicants

traverse these rejections. A claim is anticipated under 35 U.S.C. § 102 only if each and every limitation as set forth in the claim is found in a single prior art reference. Applicants do not believe that Kopf-Sill or any other reference teaches or suggests each and every limitation in the rejected claims, for at least the following reasons.

A. The Examiner Must Consider the Entirety of the Claim

Applicants suggest that the examiner has selected portions of the Kopf-Sill reference in attempt to find correspondence with selected elements of the claim. However, a claim is anticipated under 35 U.S.C. § 102 only if each and every element as set forth in the claim is found in a single prior art reference.

The Examiner asserts that Kopf-Sill discloses a particulate mass label, and cites col. 28, lines 4-5. However, this portion of the reference clearly is directed to detectable (e.g., fluorescent, radioactive, enzymatic, etc.) labels, not mass labels, for assay components:

"Useful labels in the present invention include fluorescent dyes (e.g., fluorescein isothiocyanate, texas red, rhodamine, and the like), radiolabels (e.g.,  $^3\text{H}$ ,  $^{125}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$ ,  $^{32}\text{P}$ ,  $^{33}\text{P}$ , etc.), enzymes (e.g., horse-radish peroxidase, alkaline phosphatase etc.) colorimetric labels such as colloidal gold or colored glass or plastic (e.g. polystyrene, polypropylene, latex, etc.) beads. The label may be coupled directly or indirectly to the a component of the assay according to methods well known in the art."

Kopf-Sill, col., 27, line 67 to col. 28, line 9. While Kopf-Sill may disclose labels that may include particles, they are not disclosed as useful as mass labels, that is, having sufficient mass to be capable of altering a measurable property of a probe by virtue of associating with the probe. Moreover, Kopf-Sill does not include any teaching or suggestion that these particles be used as mass labels. Rather, the detectable labels of Kopf-Sill are disclosed as useful labels for direct detection.

The Examiner asserts that Kopf-Sills discloses a mass label coupled to a molecule at col. 28, lines 14-20 and lines 29-31, and that the mass label may be coupled directly or indirectly to a component of the assay (at col. 28, lines 4-8). Again, applicants suggest that Kopf-Sills describes here a detectable label, useful for direct detection, not a mass label.

The Examiner additionally asserts that the “first reactant” of Kopf-Sill (at col. 30, lines 31-46) corresponds to a probe having a measurable property that is sensitive to the size of the complex formed by binding of the mass label, probe, and the member, member-analyte complex, or member product. The first reactant is described by Kopf-Sills as follows:

“In the assays of the invention, a first reactant or assay component is contacted to a second reactant or product, typically to form a product. The reactants or components can be elements of essentially any assay which is adaptable to a flowing format; thus, while often described in terms of enzyme-substrate or receptor-ligand interactions, it will be understood that the reactants or components herein can comprise a moiety derived from any of a wide variety of components, including, antibodies, antigens, ligands, receptors, enzymes, enzyme substrates, amino acids, peptides, proteins, nucleosides, nucleotides, nucleic acids, fluorophores, chromophores, biotin, avidin, organic molecules, monomers, polymers, drugs, polysaccharides, lipids, liposomes, micelles, toxins, biopolymers, therapeutically active compounds, molecules from biological sources, blood constituents, cells or the like.”

In other words, the Examiner is suggesting that the detectable label of Kopf-Sills is not a detectable label, but a particulate mass label, and that the first reactant of Kopf-Sills is not a reactant, but a detectable label. The rationale for this analysis is the Examiner’s statement that “the binding of the mass label, probe and member (or member-analyte complex or member product), will necessarily change the size of the complex, and that the size of the complex being a measurable property.”

Applicants have several objections to this analysis. First, applicants suggest that this represents a tortured reading of Kopf-Sills, in contradiction to the plain teaching of the reference itself. Second, applicants suggest that the interpretation of the reference by the Examiner still fails to satisfy each and every element recited in claim 83, as the claim clearly states that “a measurable property of the probe is sensitive to the size of the complex.” Applicants respectfully suggest that while the size of the entire complex may be a measurable property, it is not a property of the probe itself that is sensitive to the size of the complex.

This counterintuitive interpretation of Kopf-Sills is rendered further problematic by the assertion of the Examiner, with respect to dependent claims 84, 85, and 86, that the particulate mass label is a glass bead, a colloidal metal, or a nanocrystal, i.e., members of the group that Kopf-Sills referred to as ‘detectable labels’. However, with respect to claims 28 and 29, wherein the probe is photoluminescent, the Examiner asserts that the detectable labels of Kopf-Sills now correspond to the probes of claim 83. Applicants suggest that this new interpretation of the reference contradicts the Examiner’s immediately prior interpretation, wherein the non-fluorescent ‘first reactant’ of Kopf-Sills was identified as corresponding to the probe of claim 83.

In the Examiner’s first reading of Kopf-Sills, a colloidal metal, bead, or nanocrystal is the claimed particulate mass label, and the first reactant is the claimed probe. However, under this reading, Kopf-Sills fails to anticipate the kits of claim 83 because the disclosed ‘probes’ fail to exhibit a property that is sensitive to the size of the resulting complex.

In the Examiner's second reading of Kopf-Sills, a colloidal metal, bead, or nanocrystal is the claimed particulate mass label, and the probe is selected from the same class of detectable labels, where the label is a fluorescent dyes. However, under this reading, Kopf-Sills fails to anticipate the kits of claim 83 because the reference fails to disclose any complexes that are or could be labeled simultaneously with both a colloidal metal, bead, or nanocrystal as well as a fluorescent dye, nor is there any suggestion in the reference to label a complex in this way.

Anticipation requires that every element of the claim be disclosed as set forth in the claim, particularly that the claim elements must be arranged in the reference as required by the claim. Applicants suggest that the Examiner has failed to satisfy this requirement of 35 U.S.C. § 102, and that Kopf-Sills therefore fails to anticipate the kits of claim 83.

B. One of Ordinary Skill Would Not Immediately Envisage the Claimed Kit

Applicants have suggested that the disclosure of Kopf-Sills fails to disclose any examples of the kit of claim 83. However, even if the Kopf-Sill disclosure provided a broad selection of probes, mass labels, and complex components from which a kit according to claim 83 could be formulated, applicants suggest that Kopf-Sills would nonetheless fail to anticipate the subject matter of claim 83.

The exceptionally lengthy disclosure of Kopf-Sills could only anticipate the invention of instant claim 83 if one of ordinary skill in the art, upon reviewing Kopf-Sills, would be able to "at once envisage" the kit of claim 83 (MPEP § 2131.02 and citations therein). Applicants suggest that one or ordinary skill would not be lead by Kopf-Sills to

"at once envisage" the kit of claim 83, as there is insufficient motivation in the reference itself to make the selections suggested by the Examiner.

Kopf-Sills discloses a variety of detection methods and detectable labels, including spectroscopic, photochemical, biochemical, immunochemical, electrical, optical, or chemical detection. However, there is no suggestion in Kopf-Sills to select from among this broad selection a particulate mass label over other disclosed detectable labels, nor is there any suggestion to employ the combination of a particulate mass label with a probe having a detectable property that is sensitive to the size of the resulting complex. In contrast, where the interaction of two assay components is to be detected, the reference specifically discloses the use of a first and second label in conjunction with fluorescence resonance energy transfer, not mass labeling (see col. 28, lines 38-44), and not the technique of fluorescence polarization.

In conclusion, for at least the reasons that it does not disclose each and every limitation in claim 83, does not disclose the limitations in the claims depending from claim 83, and fails to lead one of ordinary skill to immediately envisage the subject matter of claim 83, Kopf-Sill fails to anticipate the subject matter of claim 83. As claims 28-30, 33-41, and 84-89 depend directly or indirectly from claim 83, applicants suggest that they are similarly not anticipated by Kopf-Sills.

#### IV. Conclusion

Applicants believe that this application is now in condition for allowance, in view of the above remarks. Accordingly, applicants respectfully request that the Examiner issue a Notice of Allowance covering the pending claims. If the Examiner has any

questions, or if a telephone interview would in any way advance prosecution of the application, please contact the undersigned attorney of record.

**CERTIFICATE OF MAILING**

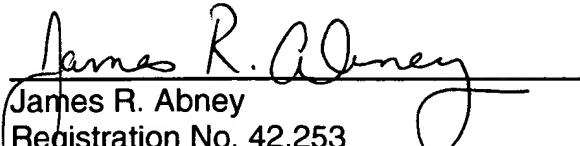
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, postage prepaid, to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450 on March 10, 2005.



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Respectfully submitted,

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